PARTICIPANT INFORMATION SHEET

FOCUS: The efficacy of xanomeline-trospium in treating cognitive impairment in psychosis: A randomised double-blind active-controlled clinical trial

Introduction

You are being invited to take part in a clinical trial aiming to find out if taking a new treatment, xanomeline-trospium (Cobenfy), can improve concentration and memory in patients with psychosis. The full scientific name of the trial is "The efficacy of xanomeline-trospium in treating cognitive impairment in psychosis: A randomised double-blind active-controlled clinical trial". You are being invited to participate in this trial because your psychiatrist has indicated that it may be desirable to change your current treatment. This is because you are still experiencing symptoms despite the treatment, or because you are getting side effects from your treatment.

Before you decide whether to take part, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the trial if you wish. Ask us if there is anything that is not clear, if you have any questions, or if you would like more information.

You do not have to participate in this trial to receive treatment for your symptoms. Your doctor can tell you more about your other options.

What is the purpose of the trial?

1. To test whether xanomeline-trospium can improve cognitive symptoms of psychosis, like poor attention and memory
2. To test whether xanomeline-trospium can improve symptoms of psychosis and daily functioning
3. To see if the side effects of xanomeline-trospium are less compared to standard antipsychotics
4. To investigate effects of xanomeline-trospium using information from Magnetic Resonance Imaging (MRI) and Magnetoencephalography (MEG) brain scans

What is xanomeline-trospium?

Xanomeline-trospium (also known as Cobenfy) is the new treatment that we are investigating in this trial. We wish to see if this new type of treatment can help the problems with memory and concentration that can affect patients with psychosis.

Drugs that are currently used in the treatment of psychosis can help to improve some of the symptoms of the disorder. However, they are less effective in improving symptoms like poor attention and memory.

An entirely new type of medication, xanomeline-trospium, has been shown to have similar beneficial effects as regular antipsychotics in improving symptoms of psychosis. In addition, xanomeline-trospium may also help to improve problems with attention and memory. Xanomeline-trospium consists of two separate compounds, xanomeline and trospium. Xanomeline is thought to have beneficial effects in the brain on psychosis symptoms. Trospium limits side effects in the rest of the body. Xanomeline-trospium is an investigational medicine and is not approved for use in the UK.

Like many medications, xanomeline-trospium can cause side effects. Xanomeline-trospium is generally well tolerated and side effects are usually mild to moderate in severity. The most common side effects are nausea, diarrhoea and constipation. The potential side effects are summarised in the section 'What are the possible risks of taking part?' and further explained in **Appendix 1** Appendix 1: OVERVIEW OF POTENTIAL SIDE EFFECTS OF XANOMELINE-TROSPIUM, **RISPERIDONE AND LURASIDONE**.

Do I have to take part?
No, participation in the trial is entirely voluntary. Your decision will not affect your clinical care or legal rights in any way. If you decide to take part, you are free to withdraw at any time; your decision to do so will not affect the care that you receive. You will be asked to inform the trial doctor should you decide to withdraw, and you do not have to give a reason for your withdrawal.

What does the trial involve?
This is a clinical trial in which xanomeline-trospium is compared to existing medication for the treatment of psychosis. The trial consists of a pre-treatment phase and a treatment phase, and an optional follow-up phase.

The pre-treatment phase starts with a screening visit during which your eligibility to participate will be assessed. There is a possibility that after screening, we may find out that you are not eligible to participate. If you are eligible, the first visit of the treatment phase will be scheduled. If you are taking any antipsychotic medication, you will also be asked to start with tapering off. During this time, you will have regular telephone check-ins to monitor your wellbeing.

During the 6-week treatment phase, we will test whether xanomeline-trospium is able to improve symptoms by comparing two groups of participants. One group of participants will be given xanomeline-trospium. The other group will be given existing medication for the treatment of psychosis, which will be the antipsychotic drug risperidone. If risperidone has already been prescribed to you in the past, or is thought not to be suitable, then lurasidone will be prescribed instead.

Whether you will be in the xanomeline-trospium or regular antipsychotic group is determined randomly by a computer (known as 'randomisation'). The computer will also randomise participants with similar characteristics to each type of treatment to create an equal number of participants in the regular antipsychotic group and the xanomeline-trospium group at each clinical site. Neither you nor the trial researchers will know which group you are in until the end of the 6-week treatment phase. However, if information about your trial treatment is clearly necessary for your appropriate medical care and where stopping the blinded trial treatment is not sufficient, your treatment allocation will be revealed.

After completing the 6-week treatment phase, you will be informed about whether you received xanomeline-trospium or a regular antipsychotic.

If you received a regular antipsychotic, your participation will end after you have completed the safety follow-up call, which will take place approximately four weeks later. Your psychiatrist will decide together with you on how to proceed with your treatment and your participation in the trial will be finished.Your psychiatrist will decide together with you on how to proceed with your treatment and your participation in the trial will be finished.

If you received xanomeline-trospium, you will have the option to decide whether you would like to continue to participate in the trial for another year. If you choose to continue, you will have three additional safety calls (every three months) and one trial visit after one year. During this time, you will remain under the care of the trial team. If you prefer not to continue, your psychiatrist will decide together with you how to proceed with your treatment, and your participation in the trial will end after the safety follow-up call.

The xanomeline-trospium and regular antipsychotics both come in capsules which are packed in blister packs. The dose will be gradually increased during the first week of the trial and can be adjusted up until the third week. The medication can be stored at room temperature. Do not store it above 30 degrees, or in the refrigerator or freezer. We ask you to return empty medication packages at each visit. More information can be found in the Participant Dosing Leaflet.

You will be asked to attend four trial visits. After Visit 1 (the screening visit), you will be contacted by phone or video call. During this call, we will discuss the next steps, including the planning for the upcoming visit. If applicable, we will also review the plan for discontinuing your current medication. At Visit 2 (the baseline visit), you will be given your trial medication to start taking the next morning.

Your trial medication dose will be gradually increased during the first week. This gradual increase follows standard medical guidelines to ensure the medication is given safely and effectively. To make sure you are tolerating the medication well, the trial team will check in with you after the first week through a video or phone call. If you experience side effects, you can also contact the study team at any time. If needed, you can reduce your dose up until your third visit in week 3. Any decision to adjust the dose will be made together with you and the trial team. If you need urgent medical care that requires knowing what medication you are taking, a study doctor is able to do this through a process called 'unblinding'. This is an emergency system that is available 24 hours a day, 7 days a week. It will only be done if this is necessary for your clinical care.

You will use the trial medication for 6 weeks. Visit 4 will take place at the end of the 6 weeks. At visit 4, you will be told which medication you received. If you received xanomeline-trospium, you will be asked whether you would like to take part in the one-year follow-up phase of the trial. During the follow-up, both you and the trial research team will know that you are taking xanomeline-trospium.

The follow-up phase includes three follow-up calls at 3, 6, and 9 months after visit 4, as well as an additional visit (visit 5) one year after visit 4. If any concerns are identified during these follow-up calls, you will be asked to attend an on-site visit so the study doctor can carry out additional checks (for example, heart rate and blood tests).

Once you have taken your final dose of trial medication of the treatment phase, a safety call will be scheduled 4 weeks after that day. This would be after visit 4 or after visit 5 if you participate in the follow up. After the 1-year follow-up period, you will not be able to continue taking xanomeline–trospium, and your future treatment will be determined by your usual NHS clinical team.

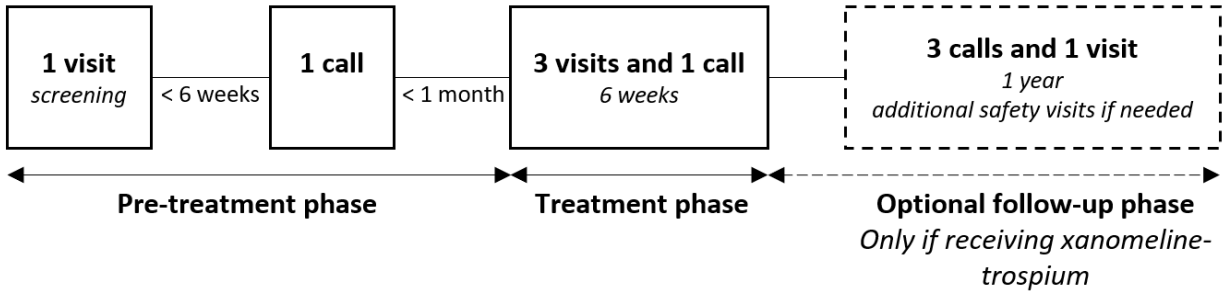

Figure 1. Overview of the different phases of the trial

You can take breaks during the visits and the longer visits (visit 1, 2, 4 and 5) can be split over multiple days if you prefer. If preferred, some of the visits can take place remotely through a video call, as long as the laboratory safety procedures can be completed by the trial team at your hospital site.

The visits will take about 2–4.5 hours each and include various activities in addition to your standard care, in short consisting of:

- Interviews and questionnaires about your symptoms, medications, and experiences
- Providing blood and urine samples
- Completing tasks/assessments on an iPad/tablet: the 'CANTAB' and 'VRFCAT' to assess thinking and memory.

None of these interviews will be audio- or video-recorded.

There are also some additional activities which you can choose to opt out of, should you decide you wish to take part in the trial:

- A session each for Magnetic Resonance Imaging (MRI) and Magnetoencephalography (MEG) brain scans. These take a maximum of 90 minutes each, and together take a maximum of 3 hours. More information about the brain scans is provided in the section 'More information about the MRI and MEG brain scans'.

If you are of childbearing potential, you will be asked to take a pregnancy test 30 days after you take the last dose of your trial medication. This pregnancy test will be provided for you at the final visit you attend, and you can take the test at home. We may remind you to take the test during the safety call and ask you to share the result with us.

You will be reimbursed for your travel expenses, time, and inconvenience related to the trial activities/visits. This will be arranged by your local trial team. Details are provided below (see "Will I be reimbursed for taking part in this trial?").

More information about each visit and procedures is provided below.

Summary of trial procedures		
When?	**What will happen?**	**Duration?**
Part 1: Pre-Treatment Phase (1-10 weeks)		
Visit 1		
	• informed consent process • explanation of what the trial involves including potential benefits and risks • opportunity to ask questions • if you agree to participate, you will be asked to sign a consent form confirming that you understand the trial and agree to take part. You will be given a copy of your consent form	2h 50m
	Assessment to ensure the trial is suitable for you	
	Questions and questionnaires about: • symptoms • medical/psychiatric/medication history • demographics • cognition	
	Computer-based tests of cognition (e.g., memory and concentration)	
	Safety checks with doctor/nurse: • blood test • physical health check including heart rate, pulse rate, respiratory rate, blood pressure, weight, height, and waist circumference • electrocardiogram heart check • urine sample for drug use screening test • urine sample for pregnancy testing (for participants of child-bearing potential)	
	Planning medication change	
Remote Contact 1		
Up to 6 weeks after Visit 1	Phone/video call to discuss discontinuing current medication and next steps	0h 20m
Part 2: Treatment Phase (6 weeks)		
Visit 2		
0 to 30 days after Remote Contact 1	Questions and questionnaires about: • symptoms • daily activities • quality of life • medication use • alcohol, smoking or other recreational drug use	2h 55m
	Computer-based tests of cognition (e.g., memory and concentration)	
	Safety checks with doctor/nurse: • blood test • physical health check including heart rate, pulse rate, respiratory rate, blood pressure, weight, height, and waist circumference • urine sample for pregnancy testing (for participants of child-bearing potential)	
	Randomisation:	

	• computer-based random allocation to the xanomeline-trospium or standard antipsychotic group (you and trial researchers will not know which treatment you have been allocated to)	
	Trial medication (xanomeline-trospium or regular antipsychotic treatment) dispensed to take home	
	Optional: MRI and MEG brain scans (additional 90 minutes each).	
Remote Contact 2		
1 week after Visit 2	Phone/video call to discuss how you are finding the medication	0h 20m
Visit 3		
3 weeks after Visit 2	Questions and questionnaires about: • symptoms • medication use and side effects • childhood experiences	2h 0m
	Repeat of safety blood tests with doctor/nurse if lab results from Visit 2 indicate additional check is needed	
	Make a decision about participating in the follow-up phase of the trial after Visit 4 and continue with trial medication for one additional year	
Visit 4		
3 weeks after Visit 3	Questions and questionnaires about: • symptoms • daily activities • quality of life • medication use and side effects	4h 25m
	Computer-based tests of cognition (e.g., memory and concentration)	
	Safety checks with doctor/nurse: • blood test • physical health check including heart rate, pulse rate, respiratory rate, blood pressure, weight, height, and waist circumference	
	Treatment unblinding: informed which treatment you received	
	Optional: MRI and MEG brain scans (additional 90 minutes each)	
Safety call		
4 weeks after final dose of trial medication	**Questions and questionnaires about:** • medication use and side effects	0h 15m
	Safety check • taking a urine pregnancy test at home 30 days after you take the final dose of trial medication (for participants of child-bearing potential)	
***Optional for participants receiving xanomeline-trospium:* Follow-up Phase (52 weeks)**		
Remote contacts 3, 4, and 5		
3, 6, and 9 months after Visit 4	**Questions about:** • medication use and side effects	0h 20m each
Visit 5		
1 year after Visit 4	Questions and questionnaires about: • symptoms • daily activities • quality of life • medication use	4h 15m

	Computer-based tests of cognition (e.g., memory and concentration)	
	Safety checks with doctor/nurse: • blood test • physical health check including heart rate, pulse rate, respiratory rate, blood pressure, weight, height, and waist circumference	
	Optional: MRI and MEG brain scans (additional 90 minutes each)	

More information about the MRI and MEG brain scans

One purpose of these brain scans is to better understand how xanomeline-trospium is working in the brain. A second purpose of the brain scans is to see whether this information can predict the changes in symptoms following treatment with xanomeline-trospium. These will happen at visit 2 (baseline), visit 4 (6 weeks after you start taking treatment) and if you take part in the optional follow-up, at visit 5 (the optional visit at 1 year after visit 4). While we would like to ask all participants to take part in the MRI and MEG brain scans, you do not have to have the brain scans to take part in the trial.

MRI

During the MRI scan, you will be asked to lie still on your back in the MRI scanner for up to 90 minutes. The MRI scanner will take some images of your brain structure and activity and will also measure the concentrations of some naturally occurring brain chemicals.

MEG

During the MEG scan, you will be asked to sit still in the MEG scanner for up to 90 minutes. Similar to the MRI scanner, the MEG scanner will take some images of your brain, focusing more on brain activity.

For further information on the MRI/MEG brain scans please see **Appendix 2**: SUPPLEMENTARY INFORMATION REGARDING THE MRI SCAN and **Appendix 3**: SUPPLEMENTARY INFORMATION REGARDING THE MEG SCAN.

More information about the blood samples

The trial involves taking blood samples. These are required should you wish to take part in the trial. We will collect a blood sample of 30 ml (2 tablespoons) at visits 1, 2, 4, and 5 to check that the trial treatment is safe for you to use and its effects on your physical health. A blood test at visit 3 will only be needed if the lab results from visit 2 indicate that an additional check is needed. These blood tests will tell us how well your liver and other organs in your body are working. The results of the safety check blood tests can be shared with you at the next trial visit. These samples will be processed as per the standard procedures at your hospital and will be destroyed once the analysis has been completed.

What should I consider?

This trial may will not be suitable for you if any of the below apply to you:

1. You have had any adverse effects related to trospium chloride in the past.
2. You are unable to be treated with either risperidone or lurasidone (as long as you are able to take one of these you can still take part).
3. You are pregnant or breastfeeding.
4. You have participated in another clinical trial in which you received an experimental or investigational drug or agent within the last 2 months.
5. You are not able to attend mandatory safety checks during the trial such as pregnancy tests (participants of childbearing potential only); safety blood tests, and reporting of side effects.

The standard antipsychotics used for comparison with xanomeline-trospium, risperidone and lurasidone, are both commonly prescribed for the treatment of psychosis. If you are randomised to risperidone, you will be given the normal recommended dose. Normally, lurasidone is taken with food to help the body absorb it better, but in this trial, it will be given without food. This is because the xanomeline-trospium must be taken without food, and we will not know which medication you are taking. To make sure that the lurasidone is still effective enough, if you are randomised to receive this medication, we will be giving you a slightly higher dose than you would normally get from routine clinical care. This higher dose is still within usual limits for treatment. The higher dose has been tested in other trials and used in routine

practice and we know that it is not harmful. If you continue taking lurasidone after the trial or in the follow-up phase of the trial, you will take it with food and you will receive the usual, slightly lower dose.

The capsules containing the xanomeline-trospium or regular antipsychotics are made with gelatine. Gelatine is a natural protein derived from an animal protein. It is often found in products like gummy candies, marshmallows, jelly, and some types of yogurts. The gelatine in the capsules is made from cow or pig. Some people choose not to eat products containing gelatine for dietary or religious reasons.

If you are of childbearing potential, you need to be willing to use highly effective contraception* during the trial and for 30 days after the last dose of your trial medication. Male participants must be willing to use a condom throughout the duration of the trial and for 30 days after taking the last dose of the trial medication.

**Highly effective methods of contraception include:*

- Hormonal forms of contraception including:
  - Combined forms (oestrogen and progestogen containing) such as the combined oral contraceptive pill (at a stable dose for at least 3 months before entering the trial), patches, or vaginal rings
  - Progestogen only forms including the progestogen-only pill, injections, implants, or an intrauterine system (IUS)
- Copper intrauterine device/coil (IUD)
- Sterilisation (fallopian tubes are blocked or sealed to prevent the eggs reaching the sperm and becoming fertilised)
- Vasectomised partner (surgical procedure to cut or seal the tubes that carry a man's sperm to permanently prevent pregnancy)
- True sexual abstinence (refraining from heterosexual intercourse during the entire period of risk associated with the trial medication)

If you do become pregnant during the trial, please stop taking the trial medication immediately and contact the trial team as soon as possible. If you become pregnant within 30 days after the last dose of trial medication, contact the trial team as soon as possible. If you are pregnant, your pregnancy will be monitored until the outcome of your pregnancy is known and we may need to review the child's medical records once to gather information about their health at birth.

What are the possible benefits of taking part?

By taking part in this trial, you will have an equal chance of receiving either xanomeline-trospium or the standard antipsychotic treatment. We hope that the xanomeline-trospium may improve memory and concentration problems. In addition, we hope that xanomeline-trospium may help control your other symptoms like hallucinations or paranoia better. This can however not be guaranteed for any of the participants on this trial.

By participating in this trial, you would be making a significant contribution to helping to develop potential new treatments for patients with psychosis, which may help improve the future treatment of those with psychosis.

What are the possible risks of taking part?

In this section, all known risks are described. You will be informed of any new risks/information by the trial team during the trial where this is relevant to you.

It is important to note that since xanomeline-trospium is a new medication it is not yet approved for use in the UK. In previous trials side effects included nausea (experienced by 19% of people), constipation (17%), indigestion (16%), vomiting (14%), high blood pressure (9%), and dry mouth (5%). There were small, temporary increases in blood pressure observed while taking xanomeline-trospium. Heart rate increases were also seen but tended to decrease with continued use. Liver function tests showed temporary increases in liver enzyme levels, mostly within the first month of starting xanomeline-trospium. However, these changes usually resolved on their own, suggesting the liver adjusts to the medication over time. Tests measuring movement showed no signs of xanomeline-trospium causing movement problems.

Xanomeline-trospium will be compared to medications that are currently prescribed for the treatment of psychosis in the UK, called risperidone or lurasidone. These medications can also cause side effects. The potential side effects of xanomeline-trospium, risperidone and lurasidone are further explained in **Appendix 1:** OVERVIEW OF POTENTIAL SIDE EFFECTS OF XANOMELINE-TROSPIUM, RISPERIDONE AND LURASIDONE.

During the trial, your treating physician and the trial team will continuously evaluate the safety of all participants. In case of safety concerns, it may be necessary to discontinue your treatment, or stop the trial as a whole.

To ensure your safety during the trial, you will regularly be required to undergo 3 mandatory safety checks during your time as a participant:

- Pregnancy tests (if appropriate) at visit 1, 2, and 30 days after your final visit
- Safety blood tests at visit 1, 2 and 4 (and at visit 3 if indicated and visit 5 if applicable)
- During each visit, you will be asked to report any adverse changes to your health or condition, any illnesses and/or untoward signs and symptoms since last being asked. This is relevant whether you believe that the changes are associated with taking xanomeline-trospium or not. This includes any suicidal thoughts, feelings or plans that you might have experienced since last being asked.

If you are unable or unwilling to have these safety checks, you will be withdrawn from the trial for your safety.

Risks of blood sampling
The risks associated with the blood sampling include pain, bleeding, bruising at the injection site and occasionally fainting in some cases. In very rare cases it can cause a local infection and hematoma (blood clot under the skin). The blood sampling will be performed by trained researchers. They will help you or refer you to related healthcare professionals if you have any discomfort or symptoms.

Potentially upsetting conversations
The researcher will ask you questions about negative personal experiences during childhood, including abuse, which you may find upsetting. If there are questions that you do not want to answer, or if you wish to stop or pause these conversations at any time, please let the researcher know. In the event that you experience distress, the visit may be paused or stopped and we also have procedures in place to ensure appropriate support is provided.

Risks of MRI scans
The MRI scanner is like a long metal cylinder (see Figure 2) and most of your body will need to go into it. Some people may find that slightly claustrophobic. As it involves magnets, people with metal in their body cannot participate. We will be able to see and talk to you throughout the scan and we will provide you with a call button, which you can press at any time if you want to come out of the scanner. The scanner

makes a loud knocking noise when it is running, so you will be given properly fitted earplugs and protective headphones during the scan. For further information about the MRI scans, please read Appendix 2.

Risks of MEG scans
The MEG scan has no clear risks associated with it. Like the MRI scan, this scan also involves magnets. Therefore, people with metal in their body cannot participate. We will ask you some brief questions to make sure it is safe for you before each MEG scan. For further information about the MEG scan, please read Appendix 3.

Will I be reimbursed for taking part in this trial?
You will be reimbursed for taking part in this trial. The total amount will depend on how many visits you attend (see below).

- £20 per visit for visits 1 to 5
- £50 per MRI scan
- £50 per MEG scan
- £50 extra for completion of the treatment phase (assessments for visits 1 to 4)
- Travel expenses will be reimbursed based on the number of miles travelled or upon submission of public transportation tickets/receipts.

You will be paid via BACS transfer or vouchers. If you receive payment via BACS transfer your bank details will be stored for 7 years in accordance with University of Oxford financial policy.

We will not pay tax or National Insurance from the money due to you. It is your responsibility to pay these and to check how any compensation received from taking part in the trial affects any state benefits to which you are entitled. Contact HM Revenue & Customs for information (http://www.hmrc.gov.uk or telephone 0300 200 3300).

What happens if there are incidental findings?
It is possible that the physical health examination or blood tests may detect an unexpected finding that is relevant to your health. In this event, we will inform your doctor, who will explain the results to you and advise on an appropriate course of action.

It is important to note that we do not carry out brain scans for diagnostic purposes, only for research. Our scans are not routinely looked at by a doctor and are therefore not a substitute for a doctor's appointment. Occasionally, however, a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor thinks that this finding is important for your current or future health, you will be contacted directly and advised to discuss it with your GP. You would not be informed unless the doctor considers the finding has clear implications for your current or future health. All information about you is kept strictly confidential.

What happens if I am admitted to hospital or have side effects?
If you decide to take part, it is important that we know if you are admitted to hospital or are unwell at any point from when you agree to take part in the trial, until the end of the trial.

We will give you a card with the contact details of the local trial team. You should keep this card with you, to let healthcare professionals know that you are taking part in this trial and inform them how to contact the trial team. It is also important that someone close to you knows that you are taking part in the trial, so that if you do get admitted to hospital, they can use the details on the card to let us know. The trial team will provide advice for you and/or the health professionals once receiving notification.

The section "What are the possible risks of taking part?" addresses the potential risks of participating in the trial, as well as the side effects of the trial treatment. If you experience any serious symptoms and need urgent advice, please contact us via the trial phone number which can be found on the card (please also see "Who do I contact if I need further information?"). You can also report any symptoms to the trial team at your next trial visit. The trial's clinical team will monitor any side effects that you report and – if required – may contact you or your doctor to discuss them.

What will happen if I do not want to continue with the trial?
If you decide to take part, you can still withdraw at any time without giving a reason. You should let us know if you wish to stop taking the trial medication but are happy to continue with the visits, or if you want to withdraw from all trial activities. Information collected up to that point will still be used in the trial. The blood and urine samples we collected from you are only used to check that it is safe and appropriate for you to participate in the trial, so these samples will be destroyed once we know the results. You or your doctor may be contacted if there are further questions regarding side effects from the trial treatment, or other aspects of safety.

If you wish to withdraw from the trial, please contact the trial team using the contact details at the end of this document. If you decide to withdraw, we will ask for a reason behind your decision, but you are not obligated to provide one. We will ask you to take part in a final safety call, which is mandatory and must take place four weeks after your last dose of trial medication. In addition, we will invite you to attend one final visit. This visit is not obligatory like the safety call, but we do recommend it for your safety. We will also ask you to return any unused trial treatment during this last visit. You will receive reimbursement for all the visits you have attended, including the reimbursement for the final visit. The decision to withdraw will not affect the standard of care you receive from the healthcare organisations in any way, now or in the future.

What happens if I forget to take my trial medication? If you forget to take a dose and more than four hours have passed, you will be advised to skip that dose and wait until the next scheduled one. If you have missed your medication for up to one week, you can simply resume by taking the next scheduled dose.

However, if you have missed taking the trial medication for more than one week, you will need to stop taking part in the treatment part of the study. Unless you decide to withdraw completely, we would still like to continue with the planned visits as originally scheduled. If you prefer not to attend any further visits, we will ask you to attend one final visit. In any case, a final safety call will take place around 4 weeks after you took your last dose of trial medication.

Who is organising and funding the trial?
The FOCUS trial is being carried out by researchers at the University of Oxford and is part of a project involving several other institutes in the UK, where a total of 150 participants will be recruited. As the University of Oxford is the research sponsor, it is legally responsible for the trial organisation and for overseeing the work of the researchers. The trial is funded by the Wellcome Trust, a charity in the UK. Xanomeline-trospium is manufactured and provided free of charge for the trial by Karuna Therapeutics, a Bristol Myers Squibb company. The regular antipsychotics (risperidone and lurasidone) are existing medications for the treatment of psychosis which are distributed by a company called Sharp. None of the investigators are employed by Karuna Therapeutics. One of the investigators received speaker/consultancy fees from Karuna Therapeutics and several other pharmaceutical companies (Janssen, Boehringer Ingelheim, and Otsuka). One of the investigators involved in this trial co-directs a company that creates digital tools to help treat mental illness.

Has the trial been approved by an ethical committee?

The XXX ethics committee has reviewed the trial for compliance with medical and ethical standards and for scientific value. This information sheet and informed consent form has been reviewed by individuals who have experienced psychosis.

Will the GP be informed of my participation in the trial?
If you participate in this trial, the investigator will inform your general practitioner (GP), your mental health team and care-coordinator. In emergencies, we may contact your GP or care-coordinator/clinical team if necessary. We will also need to access information from your medical records and from your clinical team.

Will my taking part in the trial be kept confidential?
Yes. Generally speaking, trial records and samples will be identified only by a trial code that will replace your name and address at the start of the trial. Please see **er**

Appendix 4: CONFIDENTIALITY **AND YOUR DATA** for further information.

What will happen to my data?
For further information, please see er

Appendix 4: CONFIDENTIALITY AND YOUR DATA

What will happen with the results of the trial?
The results of the trial will be published in scientific or medical journals and presented at conferences. You will not be identified in any report, presentation, or publication. Some of the research being undertaken will also contribute to the fulfilment of an educational requirement (e.g., a doctoral thesis).

Who do I contact if I need further information?
If you have any questions about the research, your rights as a participant, or would like to report any problem or injury arising from the research, please contact:

Name doctor, the investigator _____
Telephone number _____

You can also ask to speak to an independent doctor who is not part of the trial but who has enough knowledge about the trial to answer your questions.

Name of independent doctor _____
Telephone number _____

What if there is a problem?
If you have a concern about any aspect of this trial, you should ask to speak to the researchers who will do their best to answer your questions [contact number]. If you remain unhappy and wish to complain formally, you can do this through the Patient Advice and Liaison Service (PALS) via [PALS@oxfordhealth.nhs.uk/contact number/email of site-specific PALS].

The investigators recognise the important contribution that volunteers make to medical research and will make every effort to ensure your safety and wellbeing. The University of Oxford, as the research sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your taking part in this trial. If something does go wrong, you are harmed during the research, and this is due to someone's negligence, then you may have grounds for a legal action for compensation. While the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The trial doctor can advise you of further clinical action and refer you to a doctor within the NHS for treatment, if necessary.

NHS indemnity operates in respect of the clinical treatment which is provided.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this trial, contact <name of investigator> <contact details (phone number & email)> or you may contact University of Oxford Research Governance, Ethics & Assurance (RGEA) on 01865 616480, or the director of RGEA at rgea.complaints@admin.ox.ac.uk.

If you want to complain about how researchers have handled your information, you should contact the research team. If you are not happy after that, you can contact the Data Protection Officer from the University of Oxford: data.protection@admin.ox.ac.uk

If you are not happy with their response or believe they are processing your data in a way that is not right or lawful, you can complain to the Information Commissioner's Office (ICO) (www.ico.org.uk or 0303 123 1113).

How have patients and the public been involved in this trial?
Members of the public were involved in reviewing the Participant Information Sheet for the trial, and changes were made based on their input. In designing this trial, we have received patient advice on the frequency of participant visits and the tests that we will carry out. Potential participants were involved in describing the inclusion and exclusion criteria and monitoring for this trial.

Where can I find the results after the trial is ended?
A description of this clinical trial will be available on ISRCTN and http://www.ClinicalTrials.gov. The website will include a summary of the results. You can search this website at any time. The results of the trial will also be published on the trial website (https://). The results may also appear in other clinical trial registries in countries in which the trial is also being conducted. None of these websites will include information that can identify you. Copies of the published results will be available to you upon request after data collection has finished and the analyses have been performed.

Thank you for considering participating in the FOCUS trial. As a participant, you will be given a copy of this information sheet and your signed consent form to keep.

Appendix 1: OVERVIEW OF POTENTIAL SIDE EFFECTS OF XANOMELINE-TROSPIUM, RISPERIDONE AND LURASIDONE

This appendix provides an overview of possible side effects linked to the medications used in this study: xanomeline-trospium (the experimental medication), risperidone, and lurasidone (both commonly prescribed antipsychotics). The list is based on what has been reported by people who have used these medications.

Before joining the trial, we will carefully check for any medical conditions or medications that could make it unsafe for you to receive one of the study treatments (known as contraindications). For a full list of these, please refer to the dosing leaflet that will be provided when you start taking the medication.

Potential side effects of xanomeline-trospium (the experimental treatment)

More than 1 out of 10 people using xanomeline/trospium experience these very common side effects:

- Nausea (feeling sick) and/or vomiting (being sick)
- Constipation
- Indigestion

Up to 1 out of 10 people using xanomeline/trospium experience these common side effects:
Headache, dry mouth, dizziness, somnolence (feeling sleepy), insomnia (trouble sleeping), diarrhoea, heartburn, abdominal pain or discomfort, blurred vision, excessive salivation, light-headedness, excessive sweating, weight gain, decreased appetite, temporary increases in blood pressure and heart rate.

Up to 1 out of 100 people using xanomeline/trospium experience these uncommon side effects:
Abdominal pain, feeling sedated, agitation, throat irritation, dysphagia (difficulty swallowing), akathisia (restlessness), increased liver enzymes, hot flashes, unstable blood pressure, cold sweats, rash, anxiety, asthenia (weakness), and back pain

Please note: It is important to be aware that since xanomeline-trospium is a new medication, it means that we don't have as much information about it as we do for the regularly prescribed antipsychotics. So, whilst the list of side effects for the regularly prescribed antibiotics (risperidone and lurasidone) may look much longer than those for xanomeline-trospium, it is because we have been using them with patients for a long time which has allowed us to put together a more complete list of side effects. Risperidone and lurasidone are used in standard care and are approved for this indication, and it is likely that you would be prescribed one of these medications if you did not go on to the trial.

Potential side effects of risperidone

More than 1 out of 10 people using risperidone experience these **very common** side effects:

- Difficulty falling or staying asleep
- Parkinsonism: slow or impaired movement, stiffness, tightness of the muscles, slow shuffling walk, a tremor while at rest, increased saliva and/or drooling, and a loss of expression on the face
- Feeling sleepy or less alert
- Headache

Up to 1 out of 10 people using risperidone experience these **common** side effects:

- Dystonia: This is a condition involving slow or sustained involuntary contraction of muscles. While it can involve any part of the body (and may result in abnormal posture), dystonia often involves

muscles of the face, including abnormal movements of the eyes, mouth, tongue or jaw. **Contact the trial team/your doctor immediately if you experience this side effect.**

- Dyskinesia: This is a condition involving muscle movements, and can include repetitive, spastic or writhing movement, or twitching. **Contact the trial team/your doctor immediately if you experience this side effect.**

Other **common** side effects include: Pneumonia, Infection of the chest (bronchitis), common cold symptoms, sinus infection, urinary tract infection, ear infection, feeling like you have the flu, weight gain or increased appetite, sleep disorder, dizziness, tremor (shaking), blurred vision, increase in heart rate, blood pressure, and shortness of breath, sore throat, cough, nosebleeds, stuffy nose, abdominal pain or discomfort, vomiting or nausea (feeling sick), constipation, diarrhoea, indigestion, dry mouth, toothache, rash, skin redness, muscle spasms, bone or muscle ache, back pain, joint pain, incontinence (lack of control of urine), swelling of the body, arms or legs, fever, chest pain, weakness, fatigue (tiredness), pain, falling down. Risperidone can also raise your levels of a hormone called 'prolactin', found in a blood test, which may or may not cause symptoms. Symptoms of high prolactin include breast swelling and/or breast discomfort and sexual dysfunction in both sexes, difficulty in getting or maintaining erections in men, leakage of milk from the breasts, missed menstrual periods, or other problems related to the menstrual cycle or fertility in women.

Up to 1 in 100 people using risperidone experience these **uncommon** side effects (**contact the trial team/your doctor immediately if you experience any of these uncommon side effects):**

- Have dementia and experience a sudden change in your mental state or sudden weakness or numbness of face, arms or legs, especially on one side, or slurred speech, even for a short period of time.
- Experience tardive dyskinesia: twitching or jerking movements that you cannot control in your face, tongue, or other parts of your body.
- Decrease in the type of white blood cells that help to protect you against infection, white blood cell count decreased, decrease in platelets (blood cells that help you stop bleeding), anaemia, decrease in red blood cells, increase in eosinophils (a type of white blood cell) in your blood. Signs may include any unexplained bruising or bleeding, sudden fever, sore throat, or mouth ulcers.

Other **uncommon** side effects include:
Infection of the breathing passages, bladder infection, eye infection, tonsillitis, fungal infection of the nails, infection of the skin, an infection confined to a single area of skin or part of the body, viral infection, skin inflammation caused by mites, allergic reaction, diabetes or worsening of diabetes, high blood sugar, excessive drinking of water, weight loss, loss of appetite resulting in malnutrition and low body weight, increased cholesterol in your blood, elated mood (mania), confusion, decreased sexual drive, nervousness, nightmares, sudden loss of blood supply to brain (stroke or "mini" stroke), unresponsive to stimuli, loss of consciousness, low level of consciousness, convulsions (fits), fainting, a restless urge to move parts of your body, balance disorder, abnormal coordination, dizziness upon standing, disturbance in attention, problems with speech, loss or abnormal sense of taste, reduced sensation of skin to pain and touch, a sensation of tingling, pricking, or numbness skin, oversensitivity of the eyes to light, dry eye, increased tears, redness of the eyes, sensation of spinning (vertigo), ringing in the ears, ear pain, atrial fibrillation (an abnormal heart rhythm), an interruption in conduction between the upper and lower parts of the heart, abnormal electrical conduction of the heart, prolongation of the QT interval from your heart, slow heart rate, abnormal electrical tracing of the hear (electrocardiogram or ECG), a fluttering or pounding feeling in your chest (palpitations), low blood pressure, low blood pressure upon standing (consequently, some people taking risperidone tablets may feel faint, dizzy, or may pass out when they stand up or sit up suddenly, flushing, pneumonia caused by inhaling food, lung congestion, congestion of breathing passages, crackly lung sounds, wheezing, voice disorder, breathing passage disorder, stomach

or intestinal infection, stool incontinence, very hard stool, difficulty swallowing, excessive passing of gas or wind, hives (or "nettle rash"), itching, hair loss, thickening of skin, eczema, dry skin, skin discoloration, acne, flaky, itchy scalp or skin, skin disorder, skin lesion, an increase of creatine phosphokinase in your blood, an enzyme which is sometimes released with muscle breakdown, abnormal posture, joint stiffness, joint swelling, muscle weakness, neck pain, frequent passing of urine, inability to pass urine, pain when passing urine, erectile dysfunction, ejaculation disorder, loss of menstrual periods, missed menstrual periods or other problems with your cycle (females), development of breasts in men, leakage of milk from the breasts, sexual dysfunction, breast pain, breast discomfort, vaginal discharge, swelling of the face, mouth, eyes or lips, chills, an increase in body temperature, a change in the way you walk, feeling thirsty, feeling unwell, chest discomfort, feeling "out of sorts", discomfort changes in the way your liver works (which shows up in blood tests), procedural pain (pain during treatment procedure).

Up to 1 in 1,000 people using risperidone experience these **rare** side effects
contact the trial team/your doctor immediately if you experience any of these rare side effects

- Experience blood clots in the veins, especially in the legs (symptoms include swelling, pain, and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty breathing.
- Experience fever, muscle stiffness, sweating or a lowered level of consciousness (a disorder called “Neuroleptic Malignant Syndrome”).
- Are a man and experience prolonged or painful erection. This is called priapism.
- Experience severe allergic reaction characterised by fever, swollen mouth, face, lip or tongue, shortness of breath, itching, skin rash or drop in blood pressure.
- Breakdown of muscle fibres and pain in muscles (rhabdomyolysis).
- Yellowing of the skin and the eyes (jaundice).
- Inflammation of the pancreas (pancreatitis).

Other rare side effects include: infection, inappropriate secretion of a hormone that control urine volume, sleep walking, sleep-related eating disorder, sugar in the urine, low blood sugar, high blood triglycerides (a fat), lack of emotion, inability to reach orgasm, not moving or responding while awake (catatonia), blood vessel problems in the brain, coma due to uncontrolled diabetes, shaking of the head, glaucoma (increased pressure within the eyeball), problems with movement of your eyes, eye rolling, eyelid margin crusting, eye problems during cataract surgery (during cataract surgery, a condition called intraoperative floppy iris syndrome (IFIS) can happen if you take or have taken risperidone), dangerously excessive intake of water, irregular heartbeat, trouble breathing during sleep (sleep apnoea), fast, shallow breathing, swollen tongue, chapped lips, rash on skin related to drug, dandruff, a delay in menstrual periods, enlargement of the glands in your breasts, breast enlargement, discharge from the breasts, increased insulin (a hormone that controls blood sugar levels) in your blood, Decreased body temperature, Coldness in arms and legs, Symptoms of drug withdrawal

Up to 1 in 10,000 people using risperidone experience these very rare side effects:
Life threatening complications of uncontrolled diabetes. Serious allergic reaction with swelling that may involve the throat and lead to difficulty breathing. Lack of bowel muscle movement that causes blockage.

Contraindications of Risperidone (Things to be careful about when taking Risperidone)

Risperidone should be used carefully if taken with other substances that affect the brain, such as alcohol, painkillers (like opiates), allergy medications (antihistamines), or calming drugs (benzodiazepines), as this can increase the risk of feeling overly tired or drowsy.

Potential side effects of lurasidone

Very common side effects (>10%)

- Feeling of restlessness and inability to sit still
- Nausea (feeling sick)
- Insomnia (trouble sleeping)

Common side effects (1-10%): Parkinsonism, speech problems, unusual muscle movements (a collection of symptoms known as extrapyramidal symptoms (EPS) which typically will involve unusual purposeless involuntary muscle movements), fast heartbeat, increased blood pressure, dizziness, muscle spasms and stiffness, vomiting (being sick), diarrhoea, back pain, rash and itching, indigestion, dry mouth or excess saliva, abdominal pain, somnolence, tiredness, agitation and anxiety, weight gain, reduced appetite, increase in creatine phosphokinase (an enzyme in muscles) seen in blood tests, increase in creatinine (a marker of kidney function) seen in blood tests.

Uncommon side effects (0.1-1%): Hypersensitivity, common cold, infection of throat and nose, decreased activity of thyroid, inflammation of thyroid, aggressive behaviour, impulsive behaviour, apathy, confusional state, depressed mood, separation of normal mental processes (dissociation), hallucinations (auditory or visual), homicidal thoughts, difficulty in sleeping, sexual desire increased or decreased, lack of energy, mental condition changes, obsessive thoughts, feeling of acute and disabling anxiety (panic attack), engage in involuntary movements that serve no purpose (psychomotor hyperactivity), hyperactivity of the muscles in the body (hyperkinesia), inability to rest (restlessness), uncontrollable urge to move legs (restless legs syndrome), uncontrollable movements of mouth, tongue and limbs (tardive dyskinesia), sleep disorder, deliberate suicidal thoughts, thinking abnormal, unsteadiness (spinning sensation), alteration of taste, memory impairment, abnormal skin sensation (paraesthesia), feeling like with a tight band around head (tension headache), migraine, difficulty of the eyes in focusing, vision blurred, increased sensitivity of hearing, palpitations, alterations in heart rhythm, blood pressure dropping upon standing up which may cause fainting, increased blood pressure, abdominal pain or disturbance, absence of or deficiency in secretion of saliva, diarrhoea, indigestion, lip dry, toothache, partial or complete absence of hair, hair growth abnormal, rash, urticaria, muscle spasms and stiffness, muscle aches, joint pains, pain in arms and legs, pain in jaw, presence of bilirubin in urine, presence of protein in urine, a marker of kidney function, pain or difficulty when passing urine, frequent urination, renal disorder, sexual dysfunction, difficulty in ejaculation, abnormal breast enlargement, breast pain, milk secretion from breasts, menstruation absent or irregular, make uncontrolled noises and movements (Tourette's disorder), chills, problems walking, malaise, chest pain, fever, intentional overdose, effects on the thyroid function, seen in blood tests increased blood cholesterol, increased blood triglycerides, decreased high density lipoprotein, decreased low density lipoprotein, seen in blood tests, increased blood glucose (blood sugar), increased blood insulin, increase in some liver enzymes seen in blood tests, increased or decreased blood testosterone, increased blood thyroid stimulating hormone, electrocardiogram alterations decreased haemoglobin, reduced levels of white blood cells (which fight infection).

Contraindications of Lurasidone (things to be careful about when taking Lurasidone)

Taking Lurasidone with certain medications can cause problems:

- With strong medications that affect how the body breaks down drugs (like ketoconazole, clarithromycin, or ritonavir): These can increase the amount of Lurasidone in your body, which could lead to unwanted effects.

- With medications that speed up how the body breaks down drugs (like rifampicin, carbamazepine, or St. John's Wort): These can lower the amount of Lurasidone in your body, making it less effective.

Appendix 2: SUPPLEMENTARY INFORMATION REGARDING THE MRI SCAN

MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). However, because they use a large magnet to work, MRI scans are not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part, as per your local hospital policy. Other procedures depending on your hospital's MRI safety review may apply. Please let us know beforehand if you wear contact lenses or glasses.

The MRI scanner is like a long metal cylinder and most of your body will need to go into it (see Figure 2). Some people may find that slightly claustrophobic. Therefore, if you suffer from claustrophobia, MRI is unlikely to be suitable for you.

Figure 2. An MRI scanner

As the MRI involves magnets, people with metal in their body cannot participate. Normally, MRI scanning for research purposes would not be performed without further investigation if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry other pieces of metal that have accidentally entered your body.

As some of the scans are noisy, you will be given earplugs, head padding or headphones to make this quieter for you.

While very rare, tattoos can occasionally warm up in the scanner. Please inform the person operating the scanner immediately if you feel any heating. If you have a new tattoo, you should not take part in a scan until 48 hours after receiving the tattoo. Preparation for the MRI may vary according to your local hospital's requirements. However, as an example you might be asked to change into pocketless and metal-free "pyjama-style" top and trousers. You might be asked to remove underwired bras (if applicable to you) although if you have a suitable sports type bra, it might be possible to wear this instead. Metal jewellery, including body piercings, must also be removed. Generally speaking, eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field produced by the MRI scanner. Lockers may be provided to secure your personal belongings and clothing;

however, arrangements may vary between hospitals. Please consult your local hospital team for further details.

It is important to note that these research scans are not a substitute for a doctor's appointment, and the trial scans are not taken for diagnostic purposes. Depending on your hospital's usual procedures, the scans may be clinically assessed by a radiologist. However, this may not always be the case, as conducting a clinical assessment of your scans is not part of the research procedures. If it is local policy for a clinical review to take place and a medically relevant finding is detected, this finding could then be passed on to your doctor. You will only be informed if the doctor makes an unexpected finding on your scan that could affect your current or future health. Your local trial team will explain the procedure at your participating hospital during the screening visit (visit 1).

All information about you is kept strictly confidential.

Appendix 3: SUPPLEMENTARY INFORMATION REGARDING THE MEG SCAN

MEG is safe and non-invasive and does not involve any ionising radiation (x-rays). Similar to MRI, MEG scans involve magnets. MEG scans are therefore not suitable for everybody. Because of this, you will be asked pre-screening safety questions to help determine if you are able to take part, as per your local hospital policy. Other procedures depending on your hospital's MRI safety review may apply.

The MEG system contains very sensitive detectors arranged around a helmet shaped hollow (see Figure 3). Brain activity is measured from a participant as they sit with their head inside this hollow. Because the magnetic signals produced by brain activity are tiny compared to those produced by the earth and electrical equipment, the scanner is in a specially built room that keeps out magnetic fields from the environment. During the MEG scan you will be in a quiet, dark room.

Figure 3. A MEG scanner

Appendix 4: CONFIDENTIALITY AND YOUR DATA

Will my taking part in the trial be kept confidential?
Yes. Generally speaking, trial records and samples will be identified only by a trial code that will replace your name and address at the start of the trial. During the trial, research data is collected using different forms which will all be gathered in an electronic data collection system. In this system, your name and address are not mentioned, but your unique trial code is mentioned instead. This process is called 'pseudonymisation'. For example, the questionnaires you complete will be labelled with your code number instead of your name. It can be matched up with the rest of the data relating to you by the code number. Only members of the trial team, and designated individuals such as the trial monitor know which code corresponds to which participant. According to local hospital requirements, additional codes or identifiers may be used for MRI/MEG scans at local hospital sites, which will be removed before transferring to the Central Trial Team (University of Oxford server). Any identifiable information attached to your blood samples will be destroyed, along with the sample, once analysis has been completed. Your local trial team will only use the document that links your name to your trial code if this is necessary to contact you.

Your age, sex (as assigned at birth) and your level of education will be collected for the trial. These data will also be labelled with your trial code number and not with your name and/or address. For demographic purposes, we would also like to ask for information such as race, country of birth, marital status and occupation. This information will help us get accurate results from the assessments that you will complete at the trial visits. They will not be used to identify you and you do not have to provide this information to take part in the trial.

Confidentiality will be maintained as far as it is possible, unless you tell us something which implies that you or someone you mention might be in significant danger of harm. In this case, we would have to inform the relevant agencies, but we would discuss it with you first.

Responsible members of the University of Oxford, site representatives and regulatory authorities may be given access to data for monitoring and/or audit of the trial to ensure that the research is complying with applicable regulations.

The results of this trial will not include any personal details that could be used to directly identify you.

What will happen to my data?
Data protection legislation requires that we, the University of Oxford (whose legal name is The Chancellor Masters and Scholars of the University of Oxford), state the legal basis for processing information about you. In the case of research, this is a 'task in the public interest'. The University of Oxford is the sponsor for this study and is responsible for looking after your information and using it properly.

We will need to use information from your GP/hospital medical records for this research project. We will share your information related to this research project with the following types of organisations: NHS Trust trial sites; Medicines and Healthcare Products Regulatory Agency. This information will include your:

- Name
- Date of birth

- NHS number
- Contact details
- GP details
- Consultant

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure by:

- Using secure storage systems
- Following strict data protection policies
- Complying with legal and ethical requirements

We may share data about you outside the UK for research related purposes:

- As part of ongoing safety monitoring, we may share anonymised summary information about any side effects you experience to support the continued safety evaluation of the study treatment.
- To support future research.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- To help monitor the study drug, information about any side effects you experience may be shared with Karuna Therapeutics, part of Bristol Myers Squibb, the organisation responsible for developing the study drug.
- Research organisations.

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- Some of the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK
- We use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website

- We do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says
- We need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing
- We have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when we legally have to. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for the minimum period of time required by the UK Clinical Trial Regulations.

What are your choices about how your information is used?
You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

If you choose to stop taking part in the study, we would like to continue collecting information about your health from your GP and/or hospital medical records. If you do not want this to happen, tell us and we will stop.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. Any brain scan images collected during the study will be stored securely on the servers of the University of Oxford's Centre for Integrative Neuroimaging. The information you provide through your assessments, medical checks, and at study visits or contact (other than any brain scan images) will be stored securely on the University of Oxford Department of Psychiatry's servers.

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK, by:

- asking one of the research team via FOCUS@psych.ox.ac.uk
- sending an email to FOCUS@psych.ox.ac.uk
- calling us on [study team number to be confirmed]
- contacting the University's Data Protection Officer data.protection@admin.ox.ac.uk
- looking at the University's privacy notice available at: How we use your personal data for research purposes | Compliance.

If you would like to find out more about the use of confidential data in research, the HRA has developed a general information leaflet which is available at: Patient data and research leaflet - Health Research Authority.

Your bank details will be stored for 7 years in accordance with University of Oxford financial policy.

A copy of the consent form from this study will be kept in your medical records for as long as those records are retained. They will keep any other identifiable information about you from this study for up to 15 years after the study has finished.

We may use third party service providers or subcontractors to help with some of the research activities we carry out (e.g., IT provision, survey provision, transcription services etc.). We may therefore share your personal data with these providers when it is necessary to do so to allow them to carry out the services we require them to provide. However, we require all our third-party providers to have appropriate security measures in place to protect your data and we only allow them to process your data for the specific purposes we have stated in our instructions.